

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Nguyen T-N, von Seidlein L, Nguyen T-V, et al. The persistence and oscillations of submicroscopic *Plasmodium falciparum* and *Plasmodium vivax* infections over time in Vietnam: an open cohort study. *Lancet Infect Dis* 2018; published online Jan 22. [http://dx.doi.org/10.1016/S1473-3099\(18\)30046-X](http://dx.doi.org/10.1016/S1473-3099(18)30046-X).

The persistence and oscillations of submicroscopic *Plasmodium falciparum* and *vivax* infections over time in Vietnam: an open cohort study - Appendix

Tables

Table S1: The frequency of *P. falciparum*, *Pf/Pv* mixed or *Pspp*. infections in relation to PCR test performed

Table S2: The frequency of *P. vivax*, *Pf/Pv* mixed or *Pspp*. Infections in relation to PCR test performed

Table S3: The duration of 638 episodes of Plasmodium infections

Figures

Figure S1: Venn diagram illustrating *P falciparum* and *P vivax* infection groups

Figure S2: The relationship of parasite density (log scale) and fever for all parasitaemias

Figure S3: The distribution of the number of surveys that the study cohort members participated in.

Figure S4: Number of group members who had uPCR tests positive for *Pf*, *Pf/Pv mixed*, or *P.spp* (with trendline)

Figure S5: The maximum parasite density (log scale) increases with duration of *Pf*, *Pf/Pv mixed*, or *P.spp* (with linear trendline).

Figure S6: *Pf*, *Pf/Pv* or *P. spp* infections - MDA on M0, M1 and M2

Figure S7: *Pf*, *Pf/Pv* or *P. spp* infections - MDA on M12, M13 and M14

Figure S8: *Pv*, *Pf/Pv* or *P. spp* infections - MDA on M0, M1 and M2

Figure S9: *Pv*, *Pf/Pv* or *P. spp* infections - MDA on M12, M13 and M14

Table S1: The frequency of *P. falciparum*, *Pf/Pv* mixed or *Pspp.* infections in relation to PCR test performed

Number of PCR tests performed/ cohort member	Total tests performed	People tested	Number of infections											Total positives	Positive tests /member	% tests positive			
			0	1	2	3	4	5	6	7	8	9	10	11	12	13			
0	0	0	0														0		
1	1	1	0	1													1	1.0	100%
2	14	7	0	6	1												8	1.1	57%
3	6	2	0	0	2												4	2.0	67%
4	32	8	0	6	1	1											11	1.4	34%
5	40	8	0	4	2	1	1										15	1.9	38%
6	96	16	0	6	4	3	2	1									36	2.3	38%
7	84	12	0	4	3	2	1	2									30	2.5	36%
8	200	25	0	5	5	5	6	3	0	1							76	3.0	38%
9	180	20	0	5	3	4	3	3	2								62	3.1	34%
10	270	27	0	6	5	6	1	5	1	0	2	1					94	3.5	35%
11	264	24	0	6	6	3	3	1	2	2	1						78	3.3	30%
12	612	51	0	9	13	8	4	5	5	1	3	2	1				189	3.7	31%
13	390	30	0	4	6	3	3	5	2	2	2	2	0	0	1		134	4.5	34%
14	406	29	0	3	8	5	1	2	0	4	2	3	0	0	0	1	132	4.6	33%
15	300	20	0	3	3	1	3	1	1	4	1	0	1	0	2		105	5.3	35%
16	304	19	0	2	1	3	3	2	0	3	1	0	2	1	1		107	5.6	35%
17	221	13	0	4	1	1	2	0	2	2	0	1					52	4.0	24%
18	198	11	0	0	1	1	2	2	1	1	0	3					63	5.7	32%
19	190	10	0	1	1	2	1	0	1	2	0	0	0	1	1		56	5.6	29%
20	240	12	0	1	1	2	2	2	1	0	0	1	1	1			63	5.3	26%
21	147	7	0	0	1	0	1	0	1	3	1						41	5.9	28%
22	44	2	0	0	0	0	1	0	1								10	5.0	23%
Total	4239	354	0	76	68	51	40	34	20	25	13	13	5	3	5	1	1367	3.9	32%

Table S2: The frequency of *P. vivax*, *Pf/Pv* mixed or *Pspp*. Infections in relation to PCR test performed

Number of PCR tests performed/ cohort member	Total tests performed	People tested	Number of infections															Total positives	Positive tests /member	% tests positive				
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18			
0	0	0	0																			0		
1	1	1	0	1																		1	1.0	100%
2	4	2	0	2																		2	1.0	50%
3	3	1	0	0	1																	2	2.0	67%
4	20	5	0	1	2	1	1															12	2.4	60%
5	20	4	0	2	0	1	1															9	2.3	45%
6	72	12	0	3	2	2	2	3														36	3.0	50%
7	56	8	0	0	1	1	3	2	1													33	4.1	59%
8	152	19	0	6	4	5	1	1	2													50	2.6	33%
9	144	16	0	5	0	1	3	5	1	1												58	3.6	40%
10	210	21	0	5	4	0	2	3	2	1	4											87	4.1	41%
11	165	15	0	2	1	2	1	3	1	2	1	1	1									76	5.1	46%
12	492	41	0	17	4	2	5	3	1	3	1	2	2	1								150	3.7	30%
13	299	23	0	6	0	1	1	0	0	3	5	1	3	1	1	1						149	6.5	50%
14	280	20	0	5	5	2	1	0	0	1	2	1	2	1								88	4.4	31%
15	255	17	0	4	2	2	1	0	1	2	0	2	2	0	1							88	5.2	35%
16	256	16	0	3	1	1	3	1	2	1	1	1	0	1	0	1						85	5.3	33%
17	153	9	0	2	0	1	2	0	1	0	1	0	0	1	0	1						51	5.7	33%
18	162	9	0	1	0	0	0	3	1	1	0	1	0	0	0	1	0	1				64	7.1	40%
19	190	10	0	2	3	0	1	0	0	0	1	0	1	0	0	0	1	0	0	0	1	63	6.3	33%
20	220	11	0	2	2	1	3	0	1													38	3.5	17%
21	147	7	0	1	0	3	0	0	1	0	0	0	0	1	0	0	1					41	5.9	28%
22	44	2	0	0	0	0	0	1	0	1												12	6.0	27%
Total	3345	269	0	70	32	27	29	28	14	17	16	9	11	6	3	3	3	0	0	0	1	1195	4.4	36%

Table S3: The duration of 638 episodes of Plasmodium infections

Group	n	Duration (IQR) in months	Range
<i>P. falciparum, Pf/Pv mixed or Pspp</i>			
90% to 100% (longest duration)	32	4(3-6)	(3-11)
75% to 90%	49	2(2-2)	(2-3)
50% to 75%	82	1(1-1)	(1-2)
0% to 50% (shortest duration)	162	0(0-1)	(0-1)
All (0% to 100%)	325	1(0-2)	(0-11)
<i>P. vivax, Pf/Pv mixed or Pspp</i>			
90% to 100% (longest duration)	31	6(6-8)	(5-20)
75% to 90%	47	3(3-4)	(3-5)
50% to 75%	78	2(2-2)	(1-3)
0% to 50% (shortest duration)	157	1(1-1)	(0-1)
All (0% to 100%)	313	1(1-3)	(0-20)
Pf +Pv (0% to 100%)	638	1(1-2)	(0-20)

Figure S1: Venn diagram illustrating *P. falciparum* and *P.vivax* infection groups

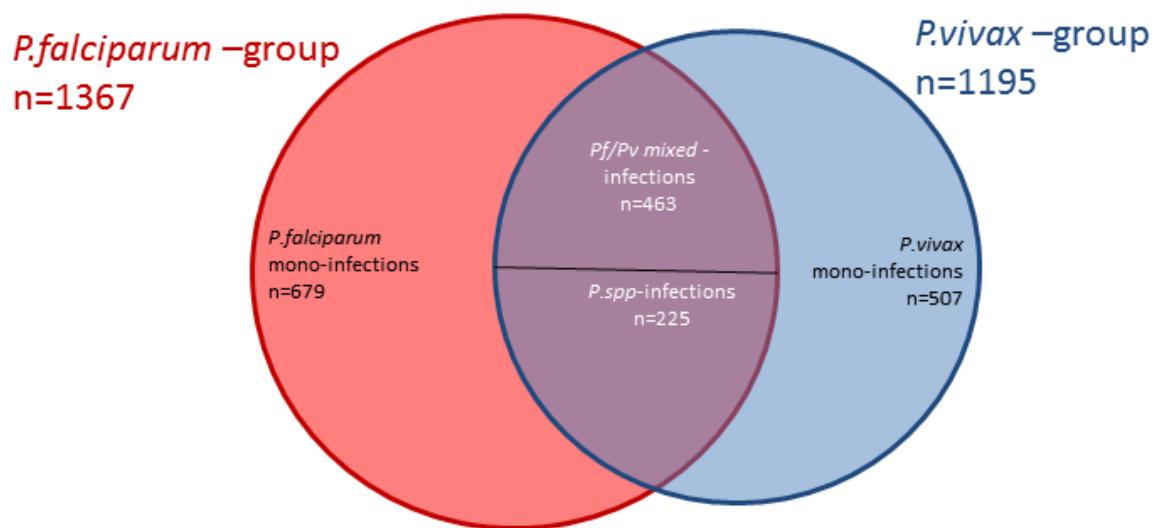
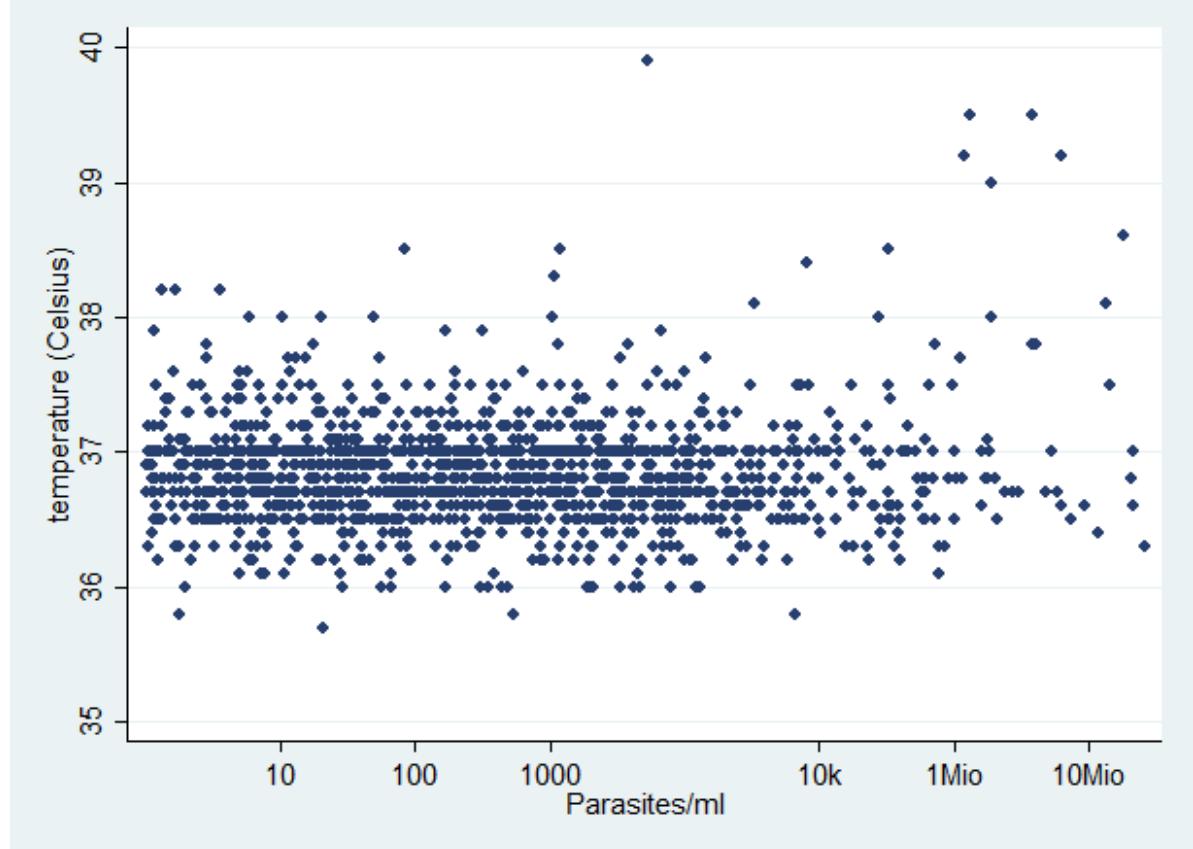
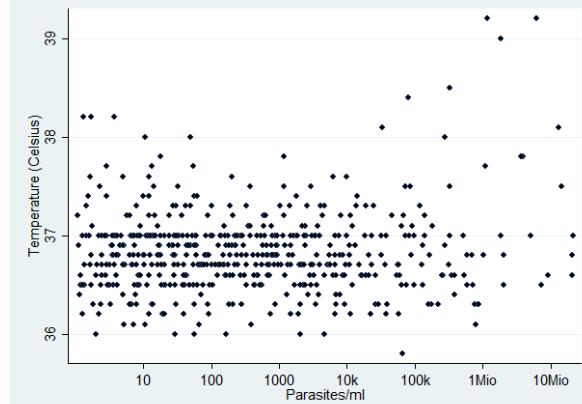


Figure S2: The relationship of parasite density (log scale) and fever for a) all parasitaemias
b) *P falciparum* mono-infections and c) for *P vivax* mono-infections

a) all parasitaemias



b) for *P falciparum* mono-infections



c) for *P vivax* mono-infections

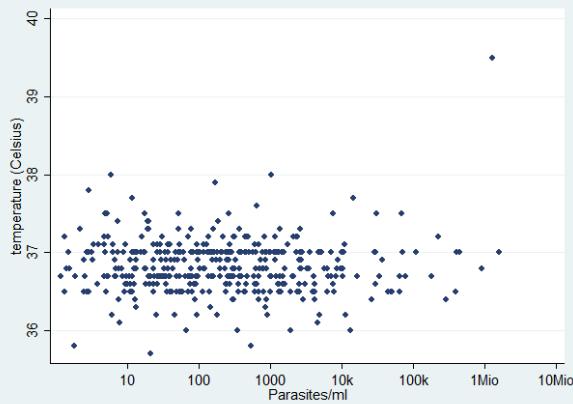


Figure S3: The distribution of the number of surveys that the study cohort members participated in.

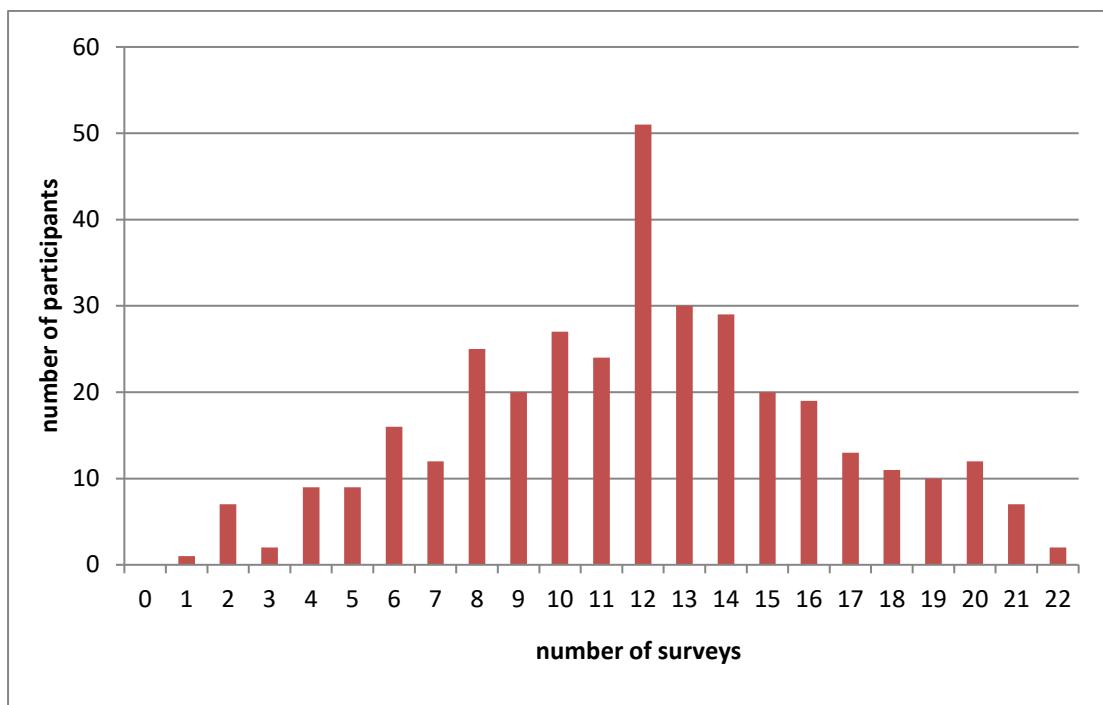


Figure S4: Number of group members who had uPCR tests positive for *Pf*, *Pf/Pv mixed*, or *P.spp* (with trendline)

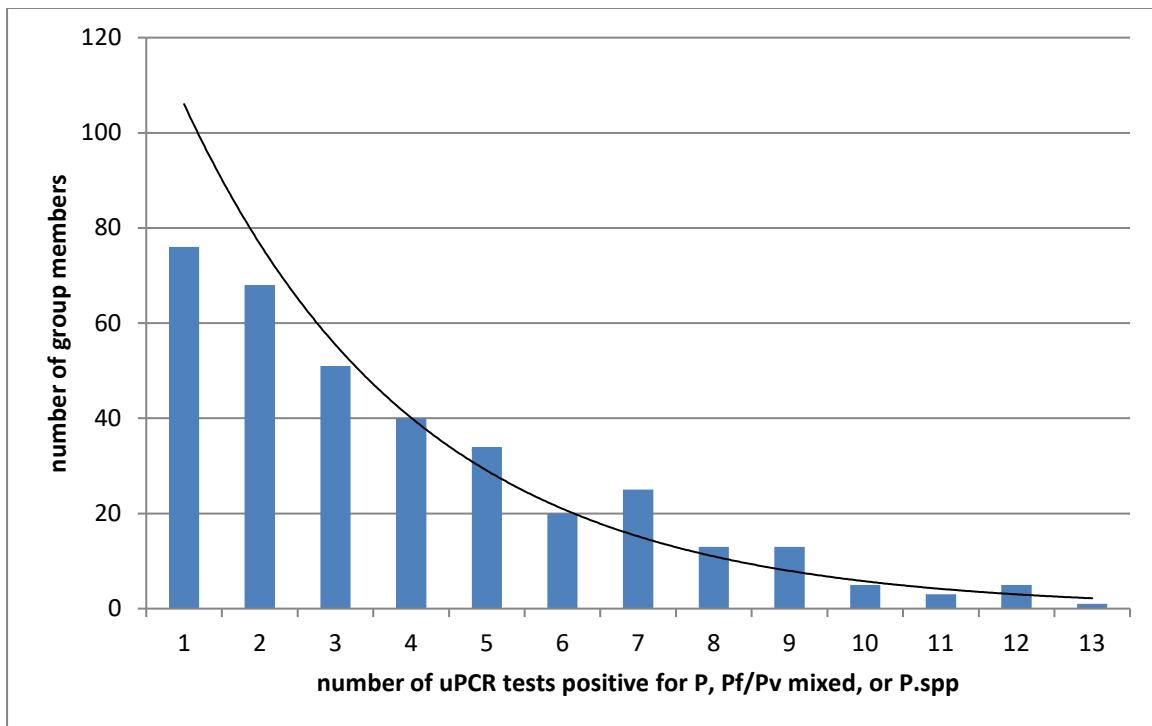


Figure S5: The maximum parasite density (log scale) increases with duration of *Pf*, *Pf/Pv mixed*, or *P.spp* (with linear trendline).

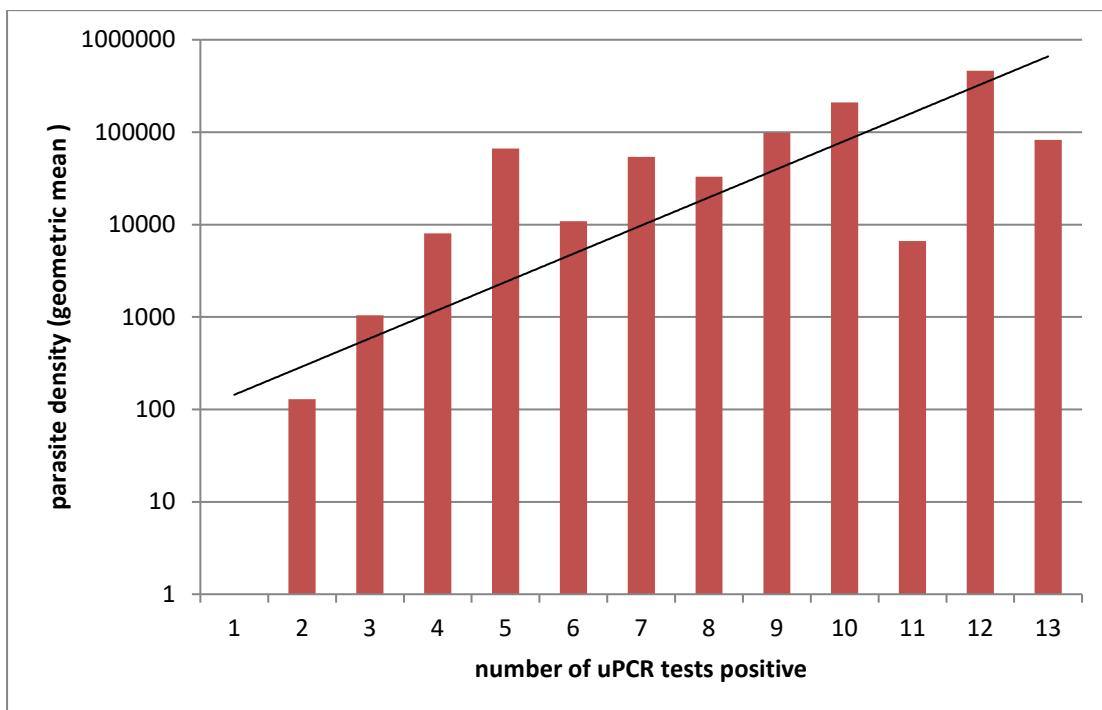
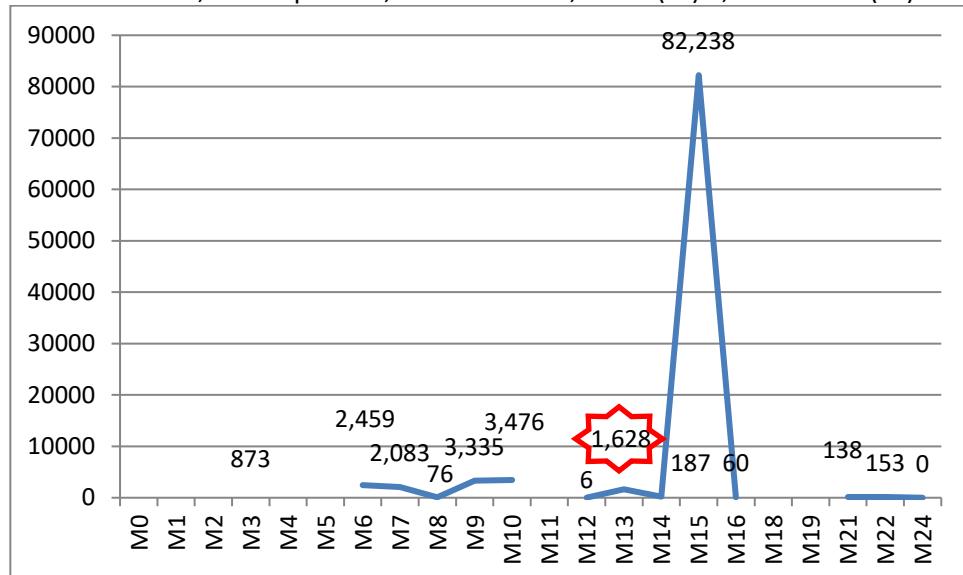


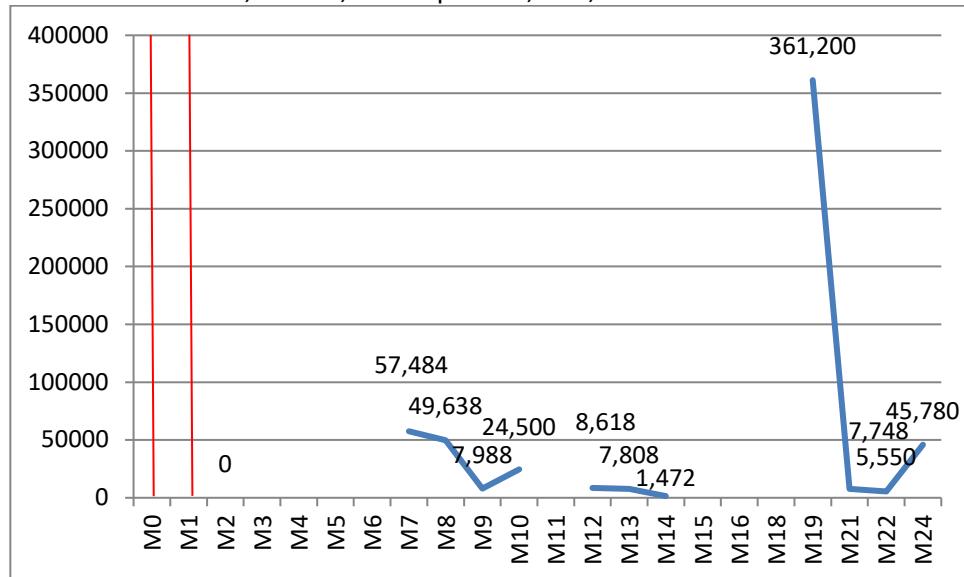
Figure S6: *Pf*, *Pf/Pv* or *P. spp* infections - MDA on M0, M1 and M2

A case series illustrating changes in parasite densities over time in 8 participants with *Pf*, *Pf/Pv* or *P. spp* infections residing in villages randomised to receive MDA on M0, M1 and M2. The number and timing of MDA(s) received by the participant is indicated by red lines. Parasite densities are provided above the respective month when the sample was collected. A febrile episode is indicated by a red star.

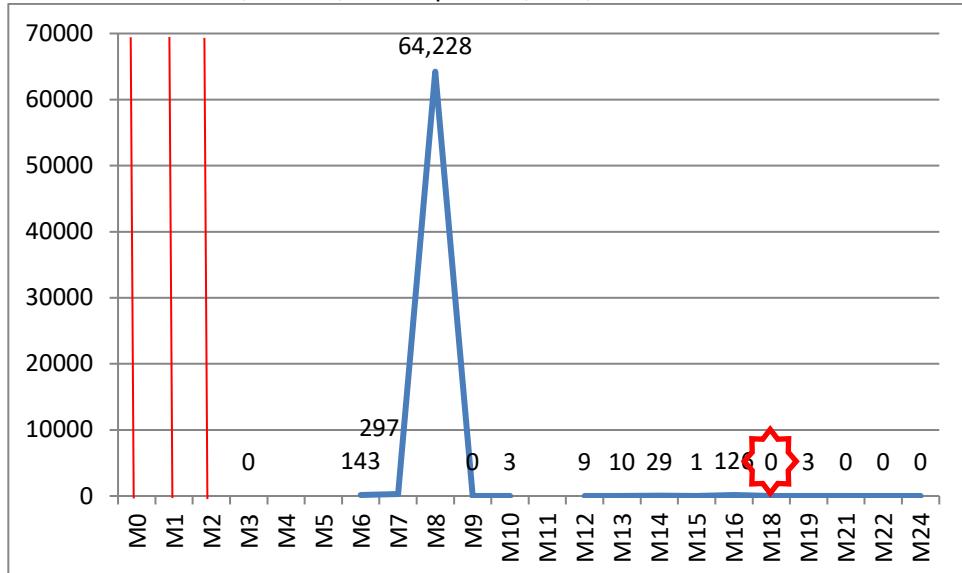
- 1 VN300493 GIA, Pf 13 episodes, MDA rounds 0, Fever (Fx) 1, Treatment (Rx) 0



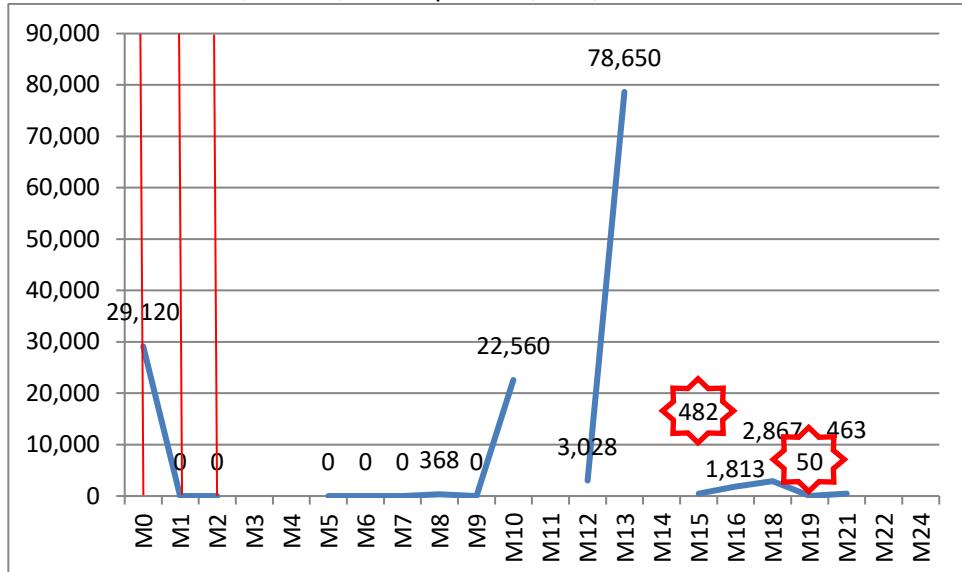
- 2 VN300694 GIA, MDA 2, Pf 12 episodes, Fx 0, Rx 0



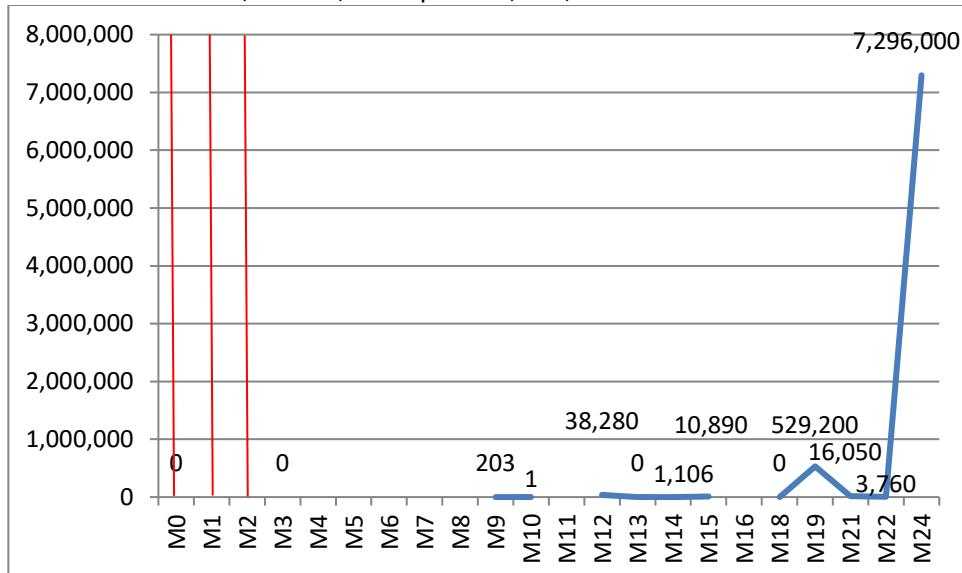
3 VN300192 GIA, MDA 3, Pf 11 episodes, Fx 1, Rx 0



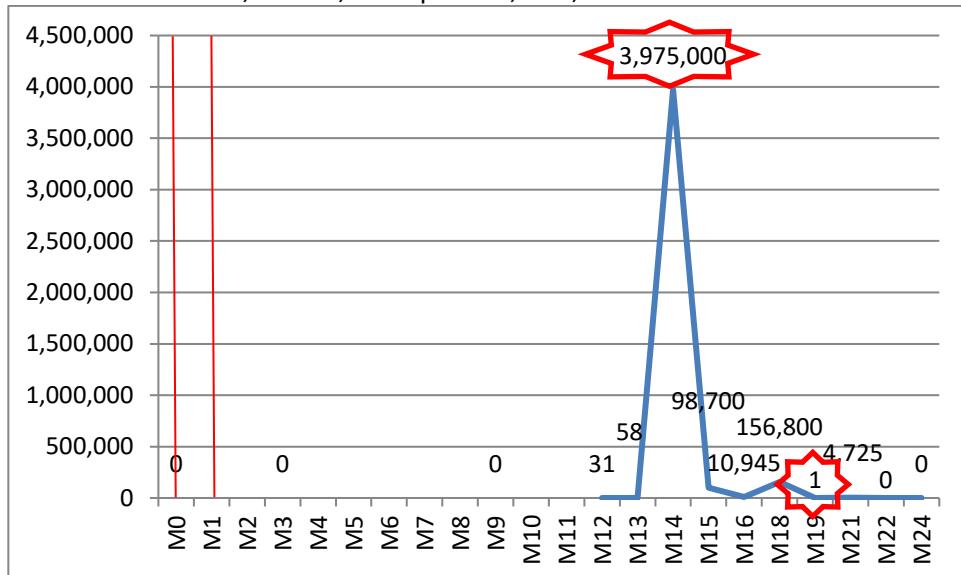
4 VN300405 GIA, MDA 3, Pf 10 episodes , Fx 2, Rx 0



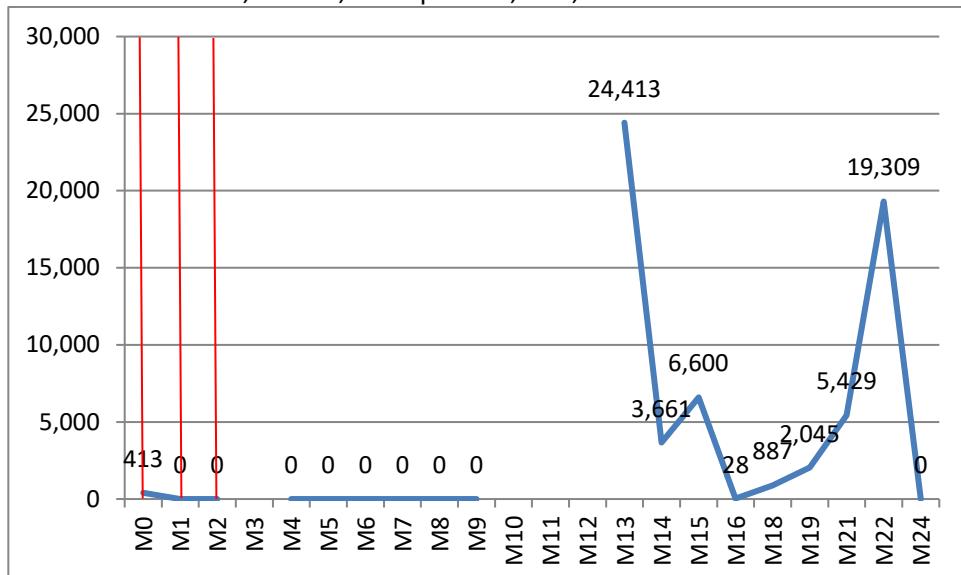
5 VN300699 GIA, MDA 3, Pf 9 episodes, Fx0, Rx 0



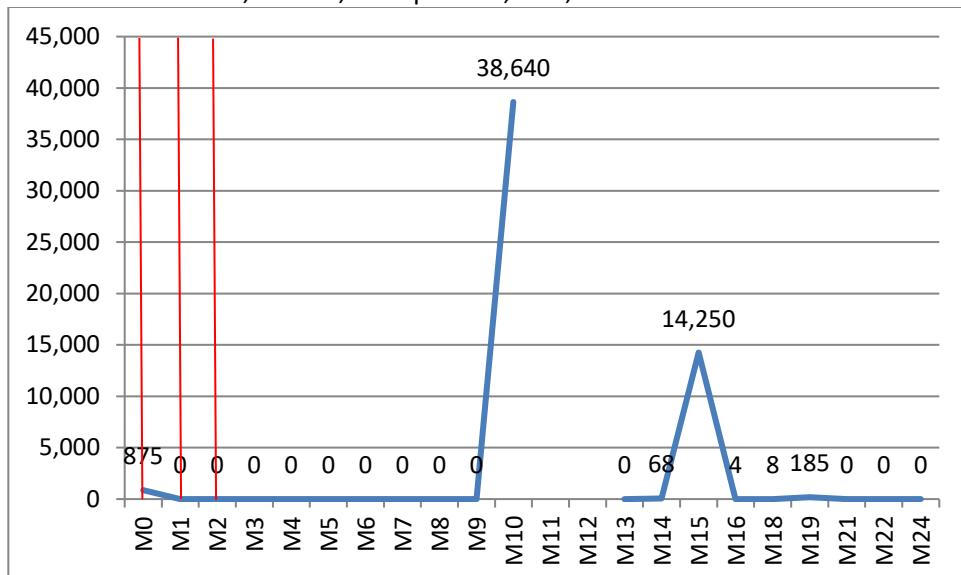
6 VN300445 GIA, MDA 2, Pf 9 episodes, Fx 3, Rx 0



7 VN300443 GIA, MDA 3, Pf 9 episodes, Fx 0, Rx 0



8 VN300485 GIA, MDA 3, Pf9 episodes, Fx 0, Rx 0

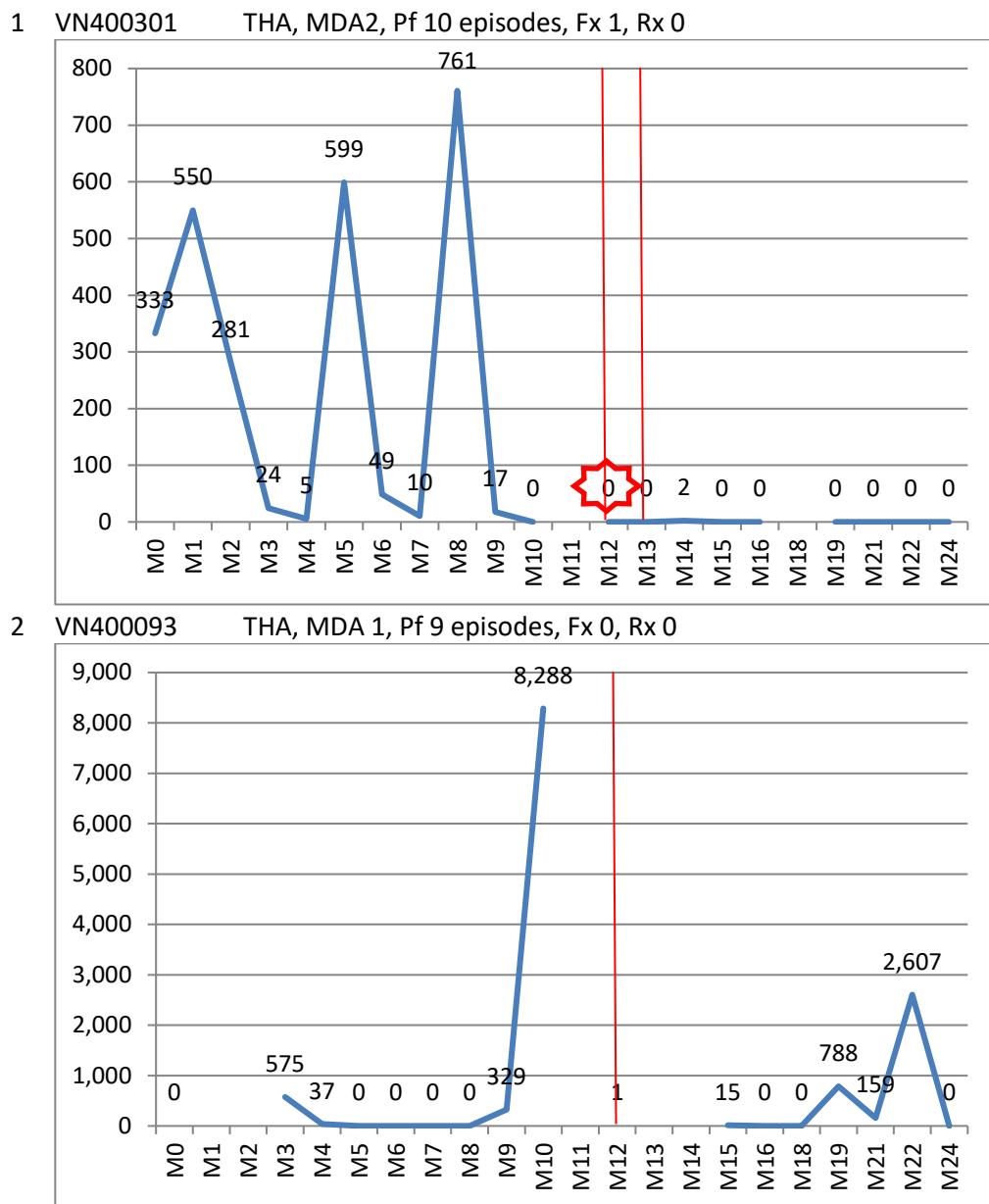


Legend:

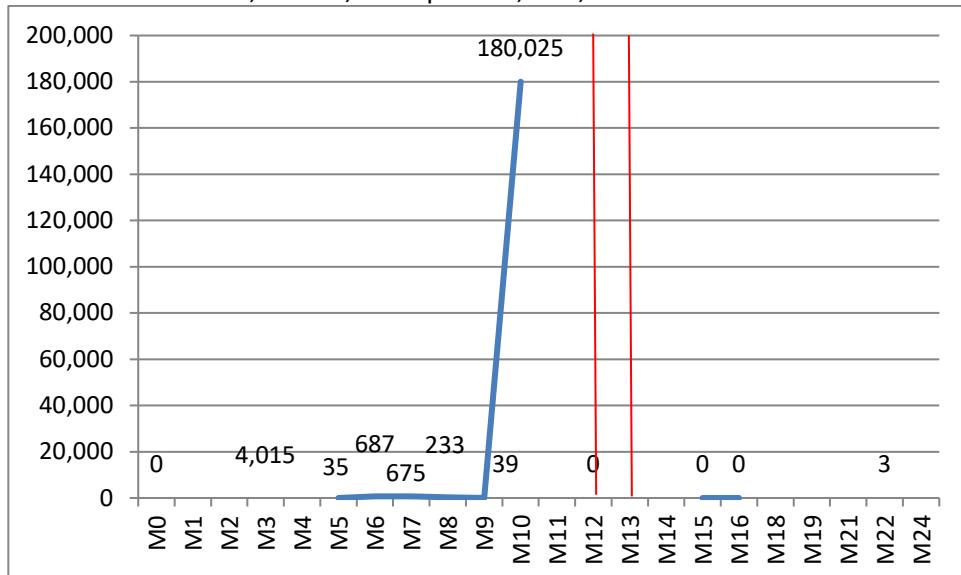
GIA = Village
MDA = Mass drug administration
Pf = *Plasmodium falciparum*
Fx = Fever episodes
Rx = Antimalarial treatment received

Figure S7: *Pf*, *Pf/Pv* or *P. spp* infections - MDA on M12, M13 and M14

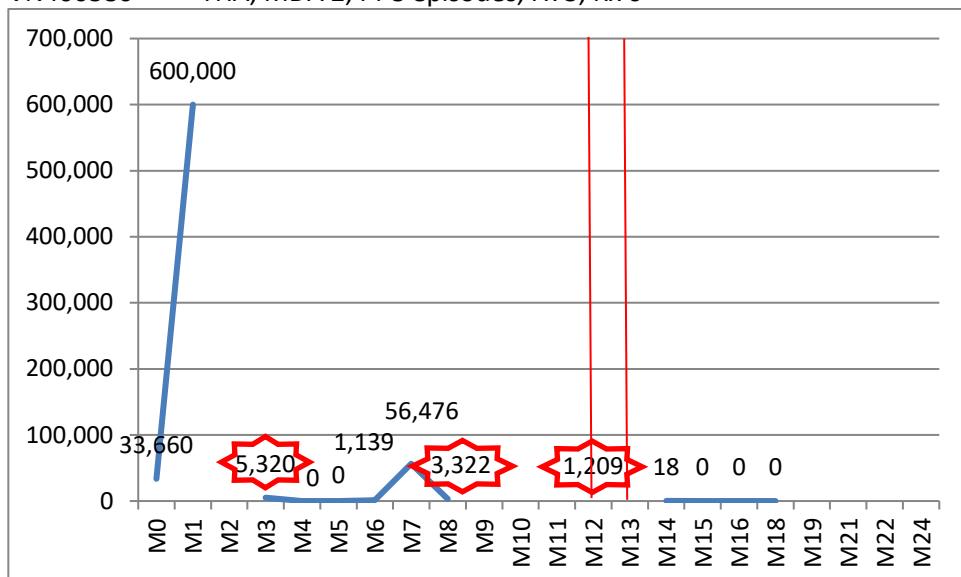
A case series illustrating changes in parasite densities over time in 4 participants with *Pf*, *Pf/Pv* or *P. spp* infections residing in villages randomised to receive MDA on M12, M13 and M14. The number and timing of MDA(s) received by the participant is indicated by red lines. Parasite densities are provided above the respective month when the sample was collected. A febrile episode is indicated by a red star.



3 VN400083 THA, MDA 2, Pf 8 episodes, Fx 0, Rx 0



4 VN400380 THA, MDA 2, Pf 8 episodes, Fx 3, Rx 0

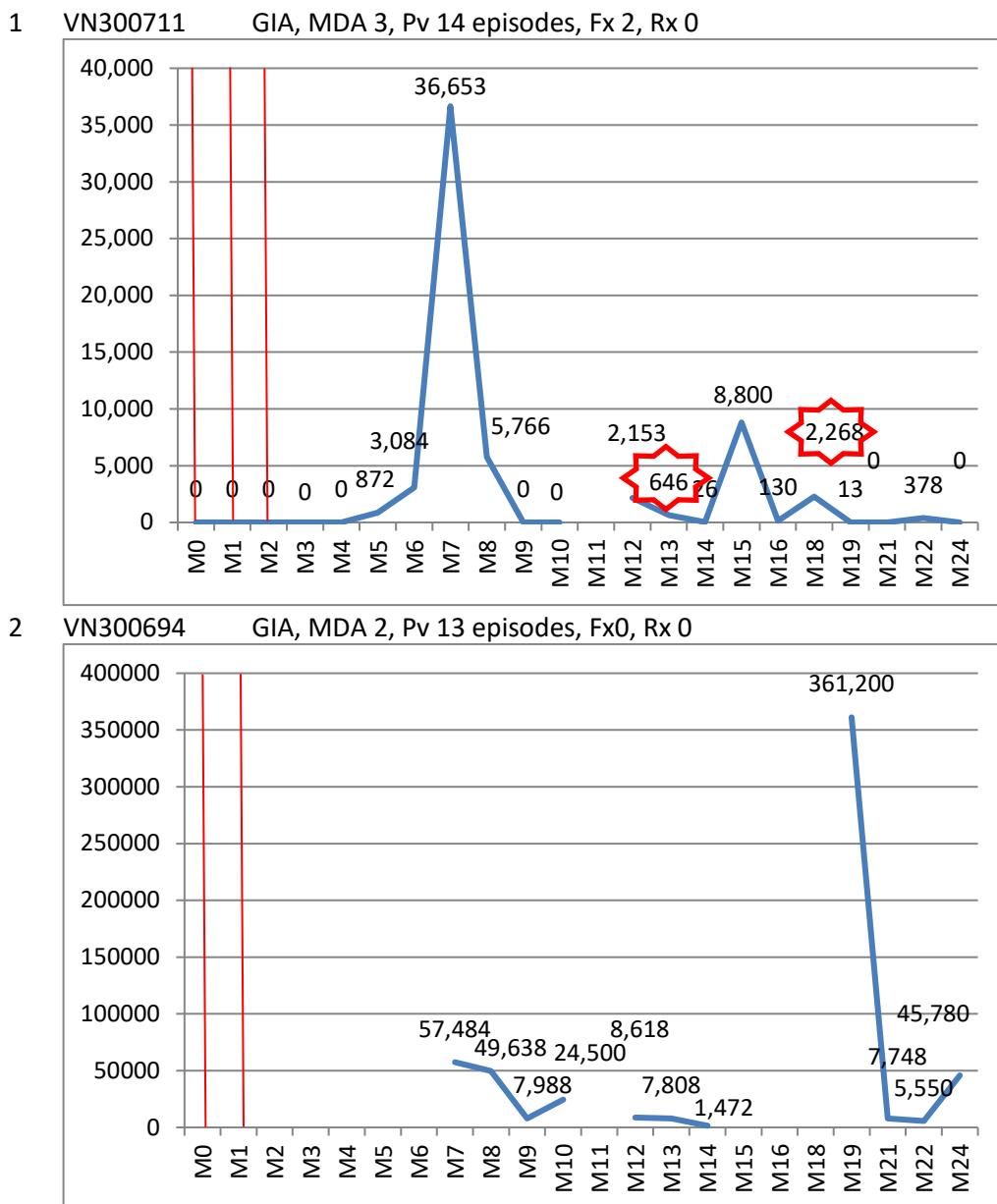


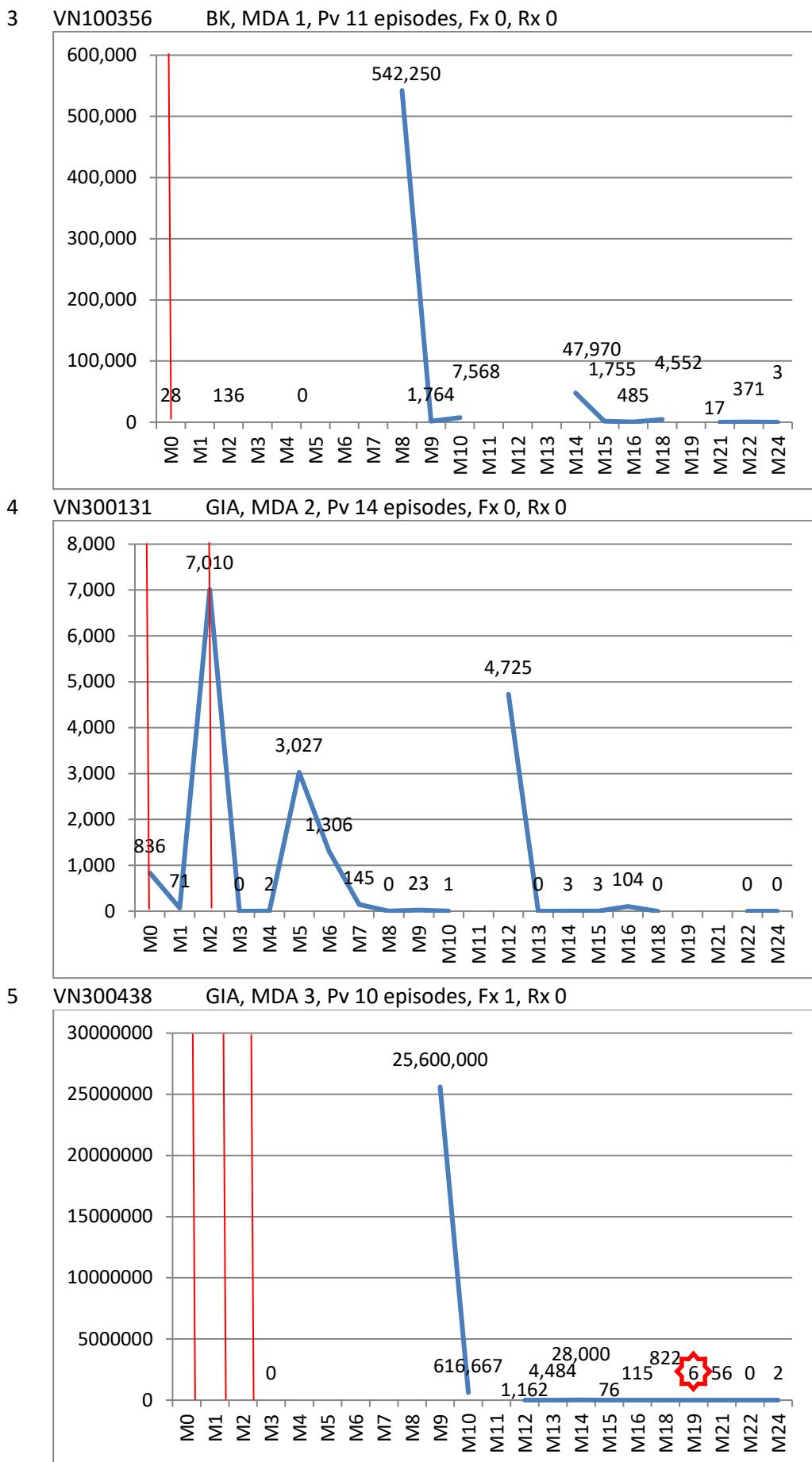
Legend:

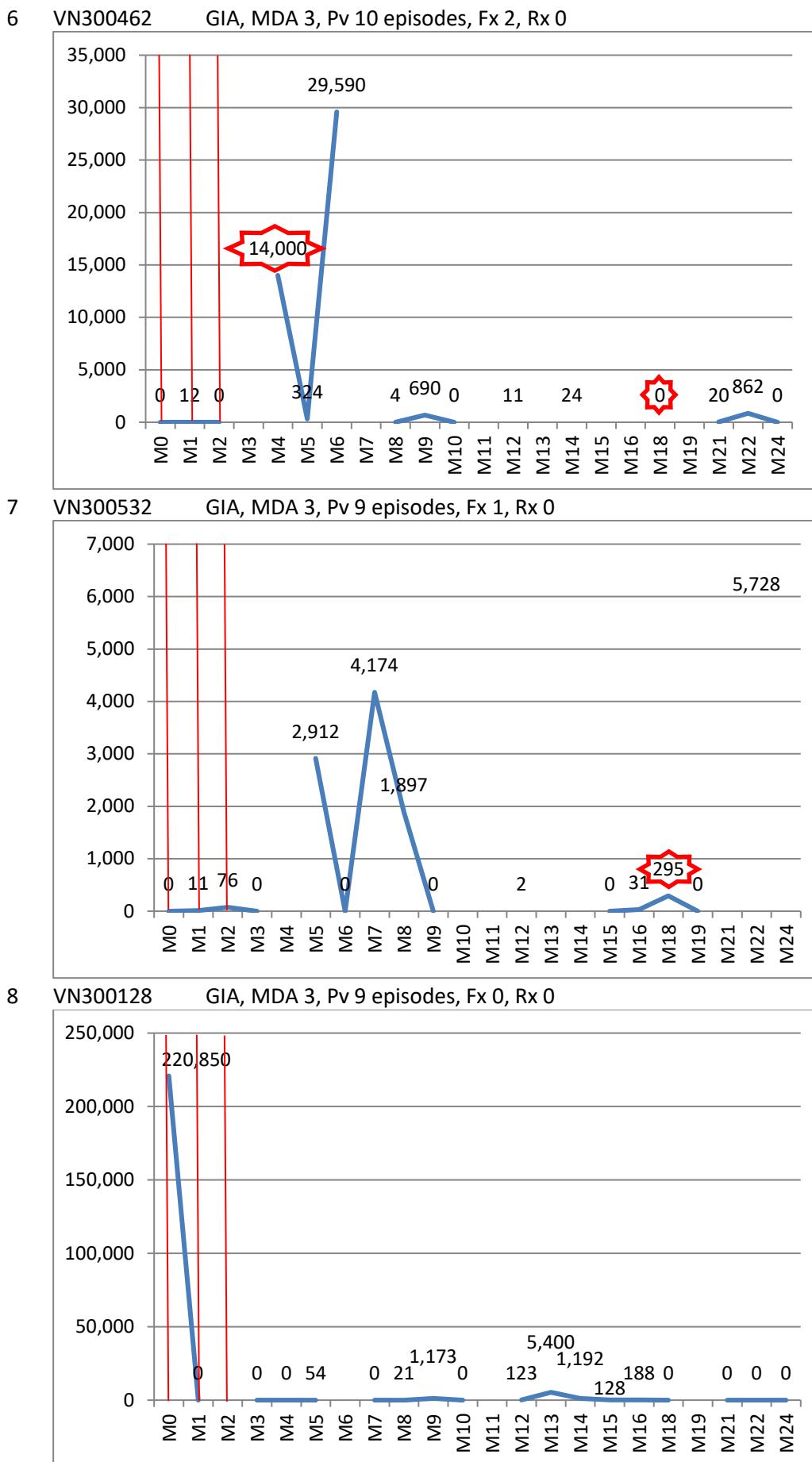
- THA = Village
- MDA = Mass drug administration
- Pf = *Plasmodium falciparum*
- Fx = Fever episodes
- Rx = Antimalarial treatment received

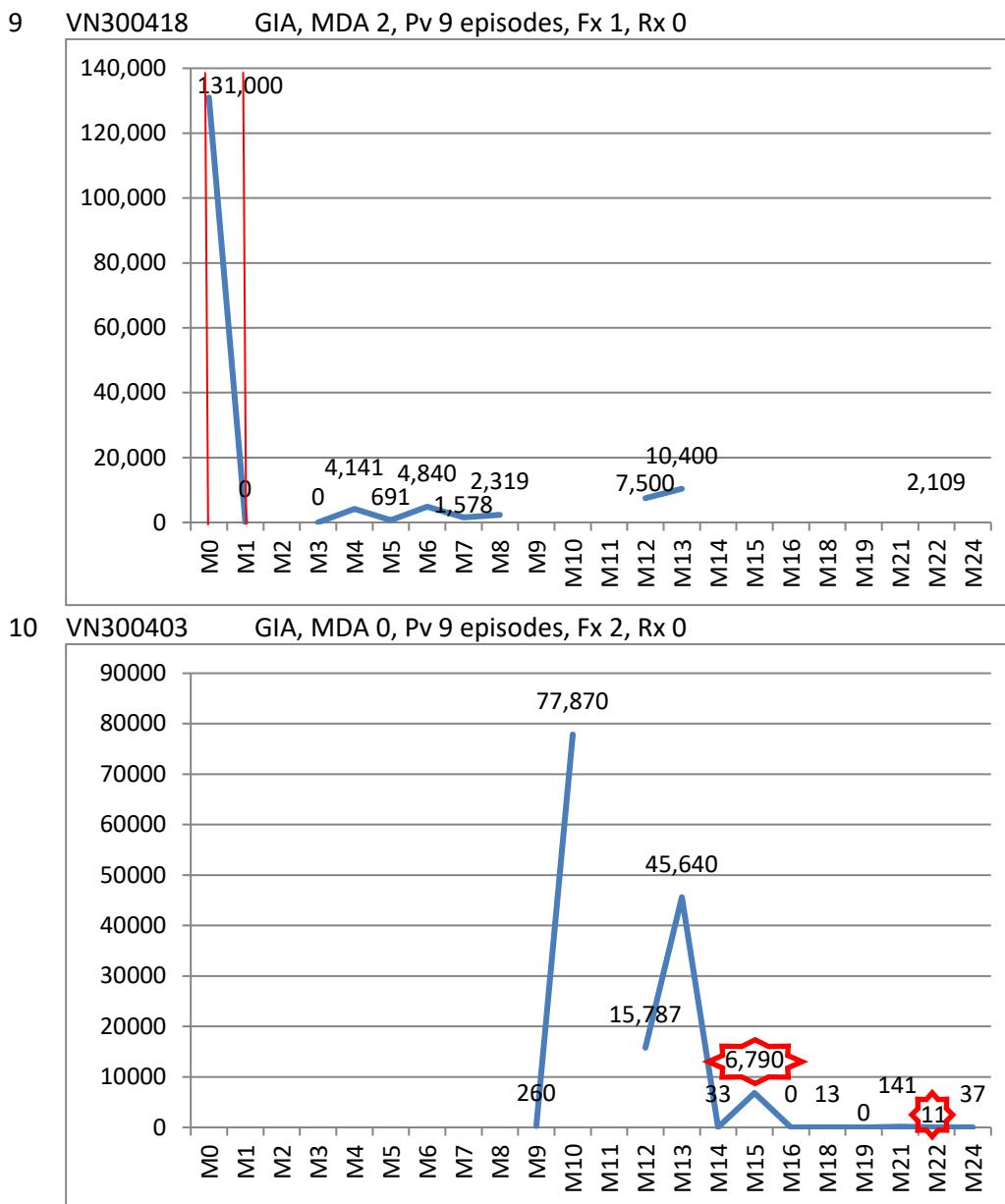
Figure S8: *Pv*, *Pf/Pv* or *P. spp* infections - MDA on M0, M1 and M2

A case series illustrating changes in parasite densities over time in 10 participants with *Pv*, *Pf/Pv* or *P. spp* infections residing in villages randomised to receive MDA on M0, M1 and M2. The number and timing of MDA(s) received by the participant is indicated by red lines. Parasite densities are provided above the respective month when the sample was collected. A febrile episode is indicated by a red star.







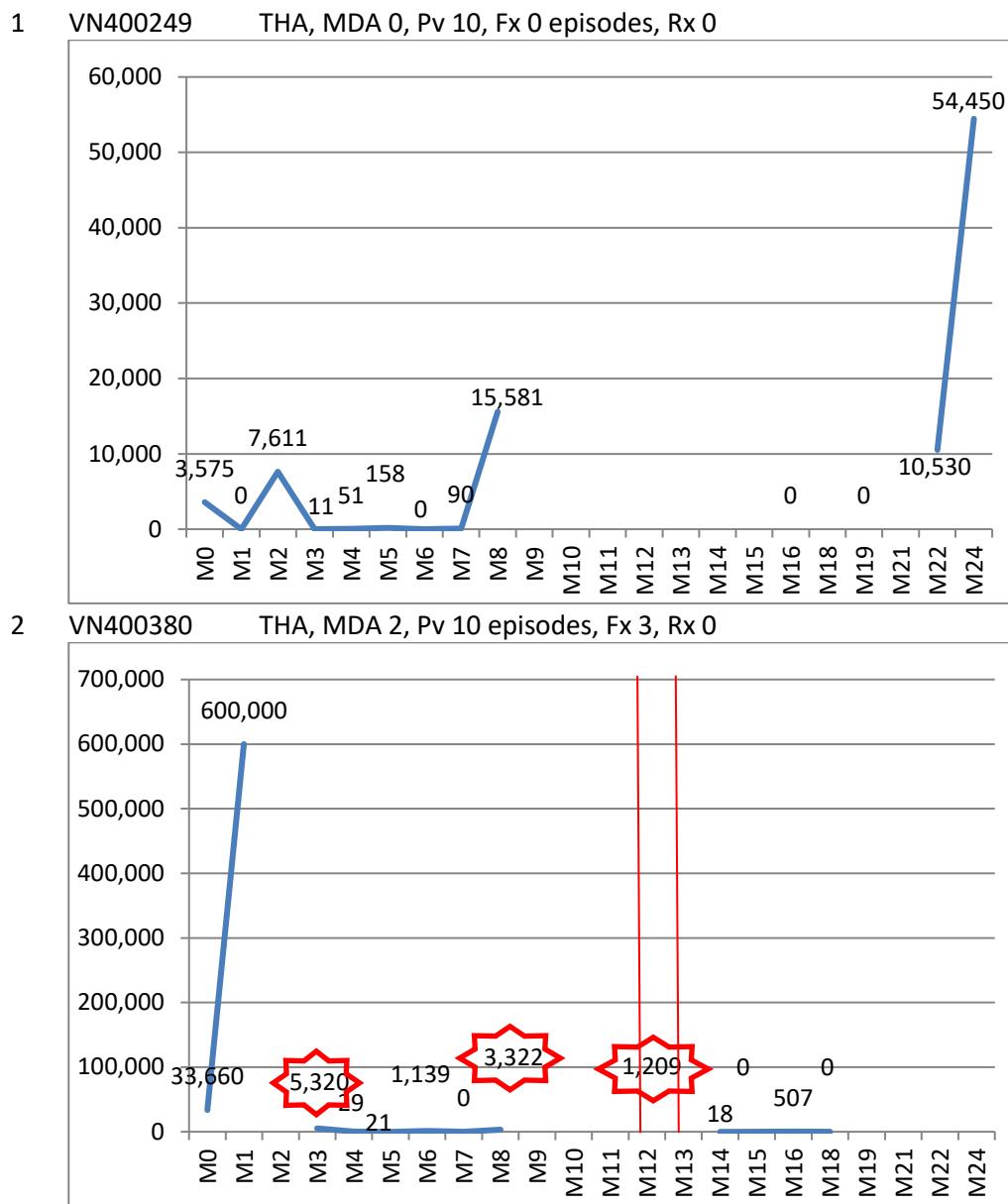


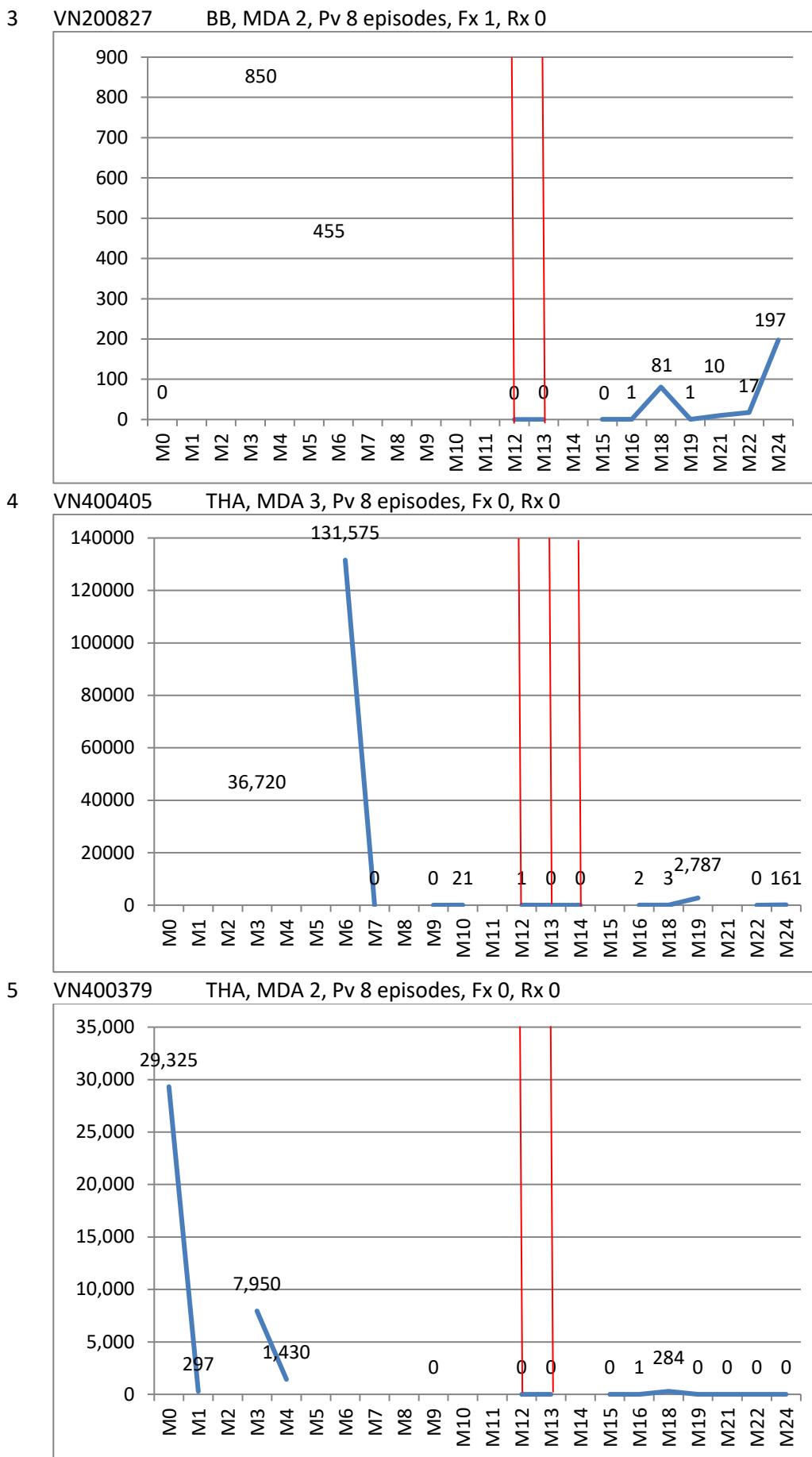
Legend:

GIA = Village
 MDA = Mass drug administration
 Pf = *Plasmodium falciparum*
 Fx = Fever episodes
 Rx = Antimalarial treatment received

Figure S9: *Pv*, *Pf/Pv* or *P. spp* infections - MDA on M12, M13 and M14

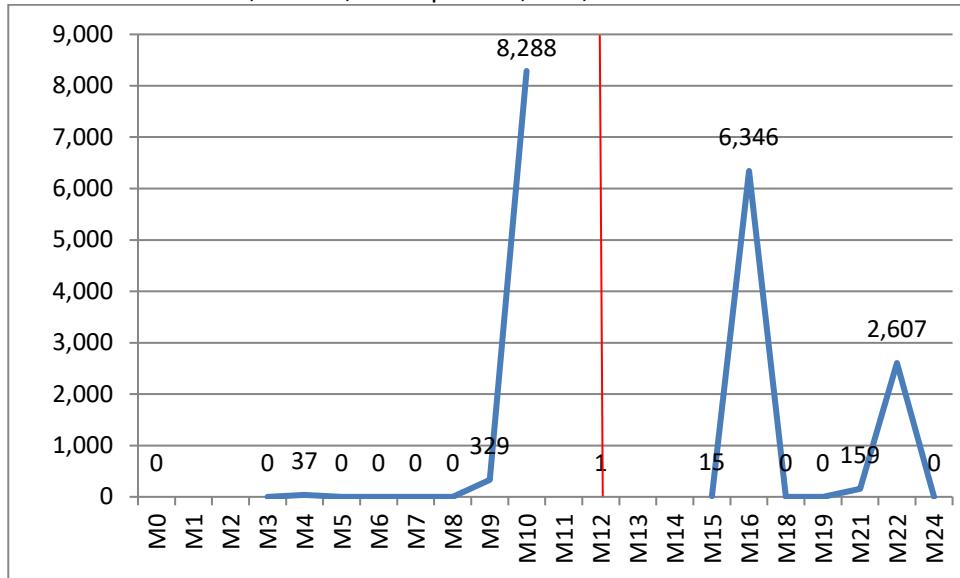
A case series illustrating changes in parasite densities over time in 6 participants with *Pv*, *Pf/Pv* or *P. spp* infections residing in villages randomised to receive MDA on M12, M13 and M14. The number and timing of MDA(s) received by the participant is indicated by red lines. Parasite densities are provided above the respective month when the sample was collected. A febrile episode is indicated by a red star.





6 VN400093

THA, MDA 1, Pv 8 episodes, Fx 0, Rx 0



Legend:

- THA = Village
MDA = Mass drug administration
Pf = *Plasmodium falciparum*
Fx = Fever episodes
Rx = Antimalarial treatment received